510(k) Summary for C.f.a.s. Proteins, C.f.a.s. PAC, PCCC, PNP, and PPP

510(k) # k133330

Applicant

The submission was prepared by Susan Hollandbeck from Roche Professional Diagnostics Regulatory Affairs and submitted on October 31, 2013.

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Candidate device

There are four candidate devices: two calibrators and two control sets.

Proprietary Names

1. C.f.a.s. (Calibrator for automated systems) Proteins
2. C.f.a.s. (Calibrator for automated systems) PAC (Prealbumin-Antistreptolysin-Ceruloplasmin)
3. PreciControl ClinChem Multi 1 and 2
4. Precinorm Protein and Precipath Protein

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Common Names

1. C.f.a.s. Proteins
2. C.f.a.s. PAC
3. PCCC
4. PNP and PPP

Submission purpose

Roche Diagnostics submits this Bundled Special 510(k) as notification of device modifications.

- All four candidate devices bear the same modification; the Antistreptolysin O analyte source material, common to the two calibrators and two controls sets, has been changed from human serum to sheep serum to eliminate conflict associated with human sourcing.
- C.f.a.s. PAC and PCCC have changed their biological additives. C.f.a.s. PAC has two fewer because they are not needed and PCCC has one more because its levels were at risk of being too low.

Measurand

There are multiple constituents for each of the four devices. They are listed in the corresponding device labeling.

Continued on next page

510(k) Summary for C.f.a.s. Proteins, C.f.a.s. PAC, PCCC, PNP, and PPP, Continued

Predicate device

The four candidate devices are modifications of the corresponding predicate devices. The device names are unchanged. They and their most recent 510(k) submissions are summarized in the table below.

Table 1: Predicate Device Clearances

Device	510(k) Submission
C.f.a.s. Proteins	K080607
C.f.a.s. PAC	K040245
PreciControl ClinChem Multi 1 and 2	K102016
Precinorm Protein and Precipath Protein	K981401

Regulatory classification of device

Table 2: Regulatory Classification of Candidate Devices

Device	C.f.a.s. Proteins and C.f.a.s. PAC	PCCC and PNP/PPP
Product Code	JIX	JJY
Device Class	II	I
Regulation	862.1150	862.1660
Description	Calibrator	Quality Control Material
Panel	Clinical Chemistry (75)	

Device description

C.f.a.s. Proteins is a liquid ready-to-use calibrator based on human serum. The concentrations of the components have been adjusted to ensure optimal calibration of the appropriate Roche methods on clinical chemistry analyzers.

C.f.a.s. PAC is a lyophilized calibrator based on human serum. The concentrations of the components have been adjusted to ensure optimal calibration of the appropriate Roche methods on clinical chemistry analyzers.

PreciControl ClinChem Multi 1 and 2 are lyophilized controls based on human serum. The adjusted concentrations and activities of the components of PCCC Multi 1 are usually in the normal range or at the normal/pathological threshold. The adjusted concentrations and activities of the components of PCCC Multi 2 are usually in the pathological range.

Precinorm Protein and Precipath Protein are liquid ready-for-use control sera based on human serum. The concentrations of the components of Precinorm Protein are usually in the normal range or at the normal/pathological threshold. The concentrations of the components of Precipath Protein are usually in the pathological range.

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510(k) Summary for C.f.a.s. Proteins, C.f.a.s. PAC, PCCC, PNP, and PPP, Continued

Intended use	The intended uses of the modified devices, as described in their labeling, have not changed as a result of the modifications. **C.f.a.s. Proteins** is for use in the calibration of quantitative Roche methods on Roche clinical chemistry analyzers as specified in the value sheets. **C.f.a.s. PAC** is for use in the calibration of quantitative Roche methods on Roche clinical chemistry analyzers as specified in the value sheets. **PreciControl ClinChem Multi 1 and 2** are for use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets. **Precinorm Protein and Precipath Protein** are for use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets.
Special conditions for use	For prescription use only
Special instruments required	These calibrators and controls are designed for use with Roche clinical chemistry analyzers in the Roche/Hitachi and COBAS INTEGRA analyzer families.

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Similarities – C.f.a.s. Proteins

The following table compares the similar features of the candidate device, C.f.a.s. Proteins, to the predicate device that was cleared in 510(k) k080607.

Table 3: Similarities between Predicate and Candidate C.f.a.s. Proteins

Feature	Predicate Device	Candidate Device
Intended use	C.f.a.s. Proteins is for use in the calibration of quantitative Roche methods on Roche clinical chemistry analyzers as specified in the value sheets.	Same
Levels	1	Same
Form	Liquid ready-to-use	Same
Matrix	Human serum with chemical and biological additives	Same
Constituents	16 constituents (complete list is in Table 11)	Same
Traceability	Traceability of the target values is given in the respective instructions for use of the system reagents.	Same
Value assignment	Traceable through master lot to reference methods or materials	Same
Unopened stability	2 – 8 °C until expiration	Same
Opened stability	4 weeks at 2 – 8 °C, provided that dispensing of the calibrator occurs without microbial contamination	Same

Differences – C.f.a.s. Proteins

The following table distinguishes the candidate device, C.f.a.s. Proteins, from the predicate device that was cleared in 510(k) k080607.

Table 4: Differences between Predicate and Candidate C.f.a.s. Proteins

Feature	Predicate Device	Candidate Device
Source material	Human Antistreptolysin O	Sheep Antistreptolysin O

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Similarities – C.f.a.s PAC

The following table compares the similar features of the candidate device, C.f.a.s. Proteins, to the predicate device that was cleared in 510(k) k080607.

Table 5: Similarities between Predicate and Candidate C.f.a.s. PAC

Feature	Predicate Device	Candidate Device
Intended use	C.f.a.s. PAC is for use in the calibration of quantitative Roche methods on Roche clinical chemistry analyzers as specified in the value sheets.	Same
Levels	1	Same
Form	Lyophilized, requires reconstitution with 1.0 mL water	Same
Matrix	Human serum with chemical and biological additives	Same
Constituents	3 constituents (complete list is in Table 11)	Same
Traceability	Traceability of the target values is given in the respective instructions for use of the system reagents.	Same
Value assignment	Traceable through master lot to reference methods or materials	Same
Unopened stability	2 – 8 °C until expiration	Same
Reconstituted stability	• 8 hours at 15 to 25 °C • 2 days at 2 to 8 °C • 2 weeks at -15 to -25 °C (when frozen once)	Same

Differences – C.f.a.s. PAC

The following table distinguishes the candidate device, C.f.a.s. PAC, from the predicate device that was cleared in 510(k) k040245.

Table 6: Differences between Predicate and Candidate C.f.a.s. PAC

Feature	Predicate Device	Candidate Device
Source material	Human Antistreptolysin O	Sheep Antistreptolysin O
Biological additives	Includes Ceruloplasmin and Prealbumin	Excludes Ceruloplasmin and Prealbumin

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Similarities – PCCC

The following table compares the similar features of the candidate device, PreciControl ClinChem Multi 1 and 2 (PCCC), to the predicate device that was cleared in 510(k) k102016.

Table 7: Similarities between Predicate and Candidate PCCC

Feature	Predicate Device	Candidate Device
Intended use	PreciControl ClinChem Multi 1 and 2 are for use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets.	Same
Levels	2	Same
Form	Lyophilized, requires reconstitution with 5.0 mL water	Same
Matrix	Human serum with chemical and biological additives	Same
Constituents	49 constituents (complete list is in Table 11)	Same
Traceability	Traceability of the target values is given in the respective instructions for use of the system reagents.	Same
Value assignment	Traceable through master lot to reference methods or materials	Same
Unopened stability	2 – 8 °C until expiration	Same
Reconstituted stability	• 12 hours at 15 to 25 °C • 5 days at 2 to 8 °C • 4 weeks at -15 to -25 °C (when frozen once) Exceptions stated for total bilirubin, direct bilirubin, UIBC, and ALT	Same

Differences – PCCC

The following table distinguishes the candidate device, PCCC, from the predicate device that was cleared in 510(k) k102016.

Table 8: Differences between Predicate and Candidate PCCC

Feature	Predicate Device	Candidate Device
Source material	Human Antistreptolysin O	Sheep Antistreptolysin O
Biological additives	Excludes Ferritin	Includes Ferritin

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Similarities – PNP/PPP

The following table compares the similar features of the candidate devices, Precinorm Protein (PNP) and Precipath Protein (PPP) to the predicate devices that were cleared in 510(k) k981401.

Table 9: Similarities between Predicate and Candidate PNP/PPP

Feature	Predicate Device	Candidate Device
Intended use	Precinorm Protein and Precipath Protein Controls are intended for use as controls in the immunoturbidimetric assay of serum proteins.	Precinorm Protein and Precipath Protein are for use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets.
Levels	2	Same
Form	Liquid ready-to-use	Same
Matrix	Human serum with chemical and biological additives	Same
Constituents	18 constituents (complete list is in Table 11)	Same
Traceability	Traceability of the target values is given in the respective instructions for use of the system reagents.	Same
Value assignment	Traceable through master lot to reference methods or materials	Same
Unopened stability	2 – 8 °C until expiration	Same
Opened stability	1 month after first opening at 2 – 8 °C providing that contamination by microorganisms is avoided.	4 weeks at 2 – 8 °C, provided that dispensing of the control occurs without microbial contamination.

Differences – PNP/PPP

The following table distinguishes the candidate devices, PNP and PPP, from the predicate devices that were cleared in 510(k) k981401.

Table 10: Differences between Predicate and Candidate PNP/PPP

Feature	Predicate Device	Candidate Device
Source material	Human Antistreptolysin O	Sheep Antistreptolysin O

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Constituents

The four candidate devices include the listed constituent analytes. The list of constituents is unchanged between candidate and predicate devices.

Table 11: Constituent Analytes of the Candidate Devices

C.f.a.s. Proteins	C.f.a.s. PAC	PNP/PPP
1. α1-Acid glycoprotein	1. Prealbumin	1. α1-Acid glycoprotein
2. α1-Antitrypsin	2. Antistreptolysin O	2. α1-Antitrypsin
3. Antistreptolysin O[1]	3. Ceroluplasmin	3. Albumin
4. C3c		4. Antistreptolysin O
5. C4		5. C3c
6. Ceruloplasmin[1]		6. C4
7. C-Reactive Protein		7. Ceruloplasmin[1]
8. Ferritin		8. C-reactive protein
9. Haptoglobin		9. Ferritin
10. IgA		10. Haptoglobin
11. IgG		11. IgA
12. IgM		12. IgG
13. Kappa[1]		13. IgM
14. Lambda[1]		14. Kappa[1]
15. Prealbumin[1]		15. Lambda[1]
16. Transferrin		16. Prealbumin[1]
		17. Total Protein
		18. Transferrin

[1]The devices are not promoted in the U.S. for these analytes.

PCCC		
1. Alanine aminotransferase	18. Ceruloplasmin	35. Lactate dehydrogenase
2. Albumin	19. Chloride	36. LDL-Cholesterol
3. Alkaline phosphatase	20. Cholesterol	37. Lipase
4. α1-Acid glycoprotein	21. Cholinesterase	38. Lithium
5. α1-Antitrypsin	22. Creatine kinase	39. Magnesium
6. Amylase	23. Creatine kinase MB	40. Phosphate
7. Amylase pancreatic	24. Creatinine	41. Potassium
8. Antisteptolysin O	25. Ferritin	42. Prealbumin
9. Apolipoprotein A-1	26. γ-Glutamyltransferase	43. Sodium
10. Apolipoprotein B	27. Glucose	44. Total protein
11. Aspartate aminotransferase	28. Haptoglobin	45. Transferrin
12. Bilirubin direct	29. HDL-Cholesterol	46. Triglycerides
13. Bilirubin total	30. IgA	47. Unsaturated iron-binding capacity
14. C-Reactive protein	31. IgG	48. Urea
15. C3c	32. IgM	49. Uric acid
16. C4	33. Iron	
17. Calcium	34. Lactate	

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Performance characteristics

These changes are supported by demonstrating no adverse impact to stability, method comparison, lower detection limit, control recovery, and precision.

Stability

The shelf life stability claim and the open vial stability claims were re-evaluated with real time stability data. Results from all timepoints tested meet the acceptance criterion.

- The acceptance criterion for C.f.a.s. Proteins, C.f.a.s. PAC, PCCC, PNP, and PPP is that the averaged results must be 90% to 110% recovery of the reference value, except...
- The acceptance criterion for Antistreptolysin O in PNP/PPP is that the average results must be 85% to 115% recovery of the reference value.

Results from all analytes from all four devices range from 91 to 108% recovery. The open vial stability claims appear in the device package inserts. They are supported with the new data. The unopened stability claim, or shelf life claim is seen by the user only as an expiration date on the device.

Method comparison

Antistreptolysin O method comparison was conducted between the candidate and predicate C.f.a.s. PAC. The Hitachi and INTEGRA analyzer families use different Antistreptolysin O reagent formulations. The **cobas c** 501 analyzer tested the Hitachi reagent formulation and the INTEGRA 800 tested the INTEGRA reagent formulation. Passing-Bablok linear regression analysis was performed on the data set of human serum samples. The x-axis was set to C.f.a.s. PAC with the current calibrator formulation; the y-axis was set to the modified one. The table below summarizes results.

Table 12: Antistreptolysin O Method Comparison Results for C.f.a.s. PAC

Test System	Criteria	Results
ASLOT **c** 501	Slope = 1.00 ± 0.10 Intercept ≤ ± 20 IU/mL R value ≥ 0.975	Slope = 1.00 Intercept = -2 IU/mL R value = 0.998
ASO I800		Slope = 1.00 Intercept = 0 IU/mL R value = 1.000

The candidate and predicate C.f.a.s. PAC compare well. Both test systems meet the criteria. There is no evidence of loss to patient sample accuracy as a result of the Antistreptolysin O source change.

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Lower detection limit	Antistreptolysin O lower detection limit (LDL) was verified using the candidate C.f.a.s. PAC to calibrate the ASLOT **cobas c** 501 test system. The LDL represents the lowest measurable analyte concentration that can be distinguished from zero. It is calculated as the value lying three standard deviations above that of the lowest standard with n =21. The study showed an LDL of 2 IU/mL which meets the criterion of ≤ 20 IU/mL, thus supported the LDL claim of 20 IU/mL.
Control recovery	Antistreptolysin O control recovery was tested with both candidate control sets on both the **cobas c** 501 and the INTEGRA 800 analyzers. Results range from 97 to 104% recovery of the target value. The acceptance criterion is 90 to 110%. All values meet the acceptance criterion. There is no evidence of loss of accuracy due to the Antistreptolysin O source change.
Precision	The potential loss to reproducibility is evaluated by testing the precision of Antistreptolysin O in both candidate control sets, PCCC and PNP/PPP, and of Ferritin in PCCC. Antistreptolysin O precision data are collected using one reagent batch on two analyzers, the **cobas c** 501 and the COBAS INTEGRA 800. Ferritin precision data are collected using one reagent batch on the **cobas c** 501 analyzer because there is no Ferritin application on the COBAS INTEGRA in the U.S. For each test system, 21 replicates were measured in a single run in a single day. The coefficient of variation (%CV) was calculated. Antistreptolysin O and Ferritin precision results range from 0 to 2% CV. All Antistreptolysin O results must produce a CV ≤ 4%. All Ferritin results must produce a CV ≤ 5%. All results meet the criterion. Therefore, there is no evidence of loss to reproducibility as a result of the device modifications.
Conclusion	The submitted information in this premarket notification supports a substantial equivalence decision. The differences between predicate and candidate do not impact the indications for use or technological characteristics.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

November 26, 2013

ROCHE DIAGNOSTICS
SUSAN HOLLANDBECK
9115 SOUTH HAGUE ROAD
INDIANAPOLIS IN 46250

Re: K133330
Trade/Device Name: C.f.a.s. PAC; C.f.a.s. Proteins; Precicontrol ClinChem Multi 1 & 2; Precinorm Protein & Precipath Protein
Regulation Number: 21 CFR 862.1150
Regulation Name: Calibrator
Regulatory Class: II
Product Code: JIX, JJY
Dated: October 31, 2013
Received: November 1, 2013

Dear Ms. Hollandbeck:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Carol C. Benson -S for

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): k133330

Device Name: **C.f.a.s. PAC**

Indications for Use:

C.f.a.s. (Calibrator for automated systems) PAC (Prealbumin-ASLO-Ceruloplasmin) is for use in the calibration of quantitative Roche methods on Roche clinical chemistry analyzers as specified in the value sheets.

Prescription Use ___X___ And/Or Over the Counter Use ____.
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostics and Radiological Health (OIR)

Ruth A. Chesler -S

Division Sign-Off
Office of In Vitro Diagnostics and Radiological Health

510(k) k133330

Indications for Use

510(k) Number (if known): k133330

Device Name: **C.f.a.s. Proteins**

Indications for Use:

C.f.a.s. (Calibrator for automated systems) Proteins is for use in the calibration of quantitative Roche methods on Roche clinical chemistry analyzers as specified in the value sheets.

Prescription Use ___X___ And/Or Over the Counter Use ____.
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

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Office of In Vitro Diagnostics and Radiological Health

510(k) k133330

Indications for Use

510(k) Number (if known): k133330

Device Name: **PreciControl ClinChem Multi 1 and 2**

Indications for Use:

PreciControl ClinChem Multi 1 is for the use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets. PreciControl ClinChem Multi 2 is for the use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets.

Prescription Use ___X___ And/Or Over the Counter Use ____
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

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Office of In Vitro Diagnostics and Radiological Health

510(k) k133330

Indications for Use

510(k) Number (if known): k133330

Device Name: **Precinorm Protein and Precipath Protein**

Indications for Use:

Precinorm Protein and Precipath Protein are for the use in quality control by monitoring accuracy and precision for the quantitative methods as specified in the value sheets.

Prescription Use ___X___ (21 CFR Part 801 Subpart D) And/Or Over the Counter Use ____. (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

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